What are the effects of maternal dietary intake of omega-3 fatty acids on breast milk composition and infant health outcomes?

Conclusion

Moderate evidence indicates that increased maternal dietary intake of long chain n-3 polyunsaturated fatty acids (PUFA), in particular docosahexaenoic acid (DHA) from at least two servings of seafood per week, during pregnancy and lactation is associated with increased DHA levels in breast milk and improved infant health outcomes, such as visual acuity and cognitive development.

Grade: Moderate

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, click here,

Evidence Summary Overview

Overall, nine articles were reviewed since 2000 to determine the effect of omega-3 fatty acids (n-3 FAs) on breast milk composition and infant health outcomes. There were seven methodologically strong prospective cohort studies conducted in the US, Europe and Canada in healthy women with low-risk pregnancies, healthy mother and infant pairs or healthy children up to eight years in cohort sizes ranging from 211 to 50,276 subjects (Drouillet, 2009; Hibbeln, 2007; Innis, 2001; Oken, 2005; Oken, 2008a; Oken, 2008b; Olsen, 2006). In addition, the evidence included one methodologically strong randomized controlled trial (RCT) of 350 mother and infant pairs in the US (Colombo, 2004) and one methodologically strong meta-analysis of 65 international studies (Brenna, 2007). For the purposes of this review, the Dietary Guidelines Advisory Committee (DGAC) excluded studies with long chain n-3 polyunsaturated fatty acids (n-3 PUFA) given in "supplement" form. Also not included were breastfeeding vs. infant formula feeding studies [before docosahexaenoic acid (DHA) addition] and studies of pre-term vs. full-term infants.

The prospective cohort studies focused on maternal DHA consumption during pregnancy and, overall, the evidence for benefits from maternal DHA consumption during pregnancy was strong. Because RCTs with DHA supplements were excluded, there were fewer studies on maternal DHA intake during lactation. However, one study examined both pregnancy and duration of breastfeeding with improved infant cognitive outcomes (Oken, 2008b) and another measured breastfeeding with associated DHA biomarkers in infants with improved cognitive outcomes (Innis, 2001).

One prospective cohort study showed that low maternal fish intake was associated with increased risk of children being in the lowest quartile for verbal intelligence quotient (IQ), and increased risk of suboptimal outcomes for fine motor skills and communication/social development scores (Hibbeln, 2007). Hibbeln et al (2007) estimated incidence of suboptimal verbal IQ in children eight years of age as a function of maternal seafood consumption during pregnancy in 11,875 women. The study was conducted in British women and analysis controlled for 28 potentially confounding variables, such as birth weight, alcohol use during pregnancy and smoking. Children of mothers reporting the highest seafood consumption, estimated using a food frequency questionnaire (FFQ) and estimated n-3 intake, were significantly less likely to score in the lowest quartile for verbal IQ compared to women who reported no seafood consumption during pregnancy.

Evidence Summary Paragraphs

Brenna et al, 2007 (positive quality) This was a meta-analysis of 65 international studies representing 2,474 women, to establish the distributions of DHA and arachidonic acid (AA) concentration in mature breast milk from mothers worldwide consuming free-living or control diets. In primary analyses, the DHA concentration was $0.32\pm0.22\%$ (range, 0.06% to 1.4%) and the AA concentration was $0.47\pm0.13\%$ (range, 0.24 to 1.0%), indicating that the DHA concentration in breast milk is lower and more variable than that of AA. The highest DHA concentrations were found primarily in coastal populations and were associated with marine food consumption. In addition, the correlation between DHA and AA was significantly low (R=0.25, P=0.02), reflecting a high degree of variability in the ratio of DHA to AA in individual breast milk samples.

Colombo et al, 2004 (positive quality) This was an RCT conducted in the US to determine the relationship between DHA levels and the development of attention measured through visual habituation during the first year of life and on measures of attention span and distraction during the second year of life. Three hundred fifty mothers and their infants were initially enrolled in a RCT for the evaluation of DHA supplementation on pregnancy outcomes; mothers' DHA intake was manipulated by providing high-DHA (13th g DHA) or ordinary (35mg DHA) eggs during the last trimester of pregnancy. Infants were seen at four, six and eight months of age for visual habitation sessions and at 12 and 18 months of age for free-play sessions in which looking to objects was measured during a single-object session and distractibility was measured during both single- and multiple-object exploration sessions. Of the 70 infants recruited from the original 350, 50 infants provided valid data at each of the three time points for the

visual habitation sessions, 58 returned for the 12-month session and 49 toddlers returned for the 18-month session. Infants whose mothers had high DHA at birth showed an accelerated decline in looking over the first year, increases in examining during single-object exploration and less distractibility in the second year. Analyses on the attention and distractibility data during toddlerhood suggest that toddlers of mothers with higher levels of DHA at birth showed more mature developmental profiles on single-object attention measures and more optimal performance on distractibility assessments than toddlers from mothers with lower DHA levels.

Drouillet et al, 2004 (positive quality) This was a prospective cohort study conducted in France to explore the relationship between seafood consumption before and during pregnancy and fetal growth, with the particular aim of assessing the possible effect of maternal overweight on this relationship. Food frequency questionnaires were completed at recruitment (before 24 weeks of gestation, concerning usual food intake in the year before pregnancy), and after the first few days following delivery (concerning food intake during the last three months of pregnancy). Of 2,002 women initially recruited (mean age 29.1±4.9 years), 1,805 women were included in the analysis and 464 were overweight. In the whole sample of women, there was no association between seafood intake and fetal growth. However, foroverweight women, higher consumption of seafood before pregnancy was associated with higher fetal biparietal and abdominal circumferences and anthropometric measures; from the lowest to the highest tertiles of intake, mean birthweight was 167g higher (P=0.002).

Hibbeln et al, 2007 (positive quality) This was an observational cohort study conducted in the United Kingdom to assess neurodevelopmental outcomes in childhood based on different levels of maternal seafood intake during pregnancy in participants of the Avon Longitudinal Study of Parents and Children (ALSPAC). Maternal seafood consumption was measured by a self-completed, non-quantitativeFFQ obtained at 32 weeks of gestation. Gross motor, fine motor, communication and social skills scales were derived from the Denver Developmental Screening Test and completed by mothers at age six, 18, 30 and 42 months. The Strengths and Difficulties Questionnaire, which included pro-social, hyperactivity, emotional symptoms, conduct problems and peer problems subscales, was completed by mothers at age 81 months. Intelligence quotient was estimated with an abbreviated version of the WISC-III, and given to children at age eight through standardized testing procedures. Of 14,541 pregnancies in the ALSPAC cohort, 13,988 children survived for at least 12 months. 8,946 infants were included at baseline, 8,801 children were included at 81 months and 5,449 children were included at eight years. After adjustment for potential confounders, maternal seafood intake during pregnancy of less than 34@ per week was associated with increased risk of children being in the lowest quartile for verbal intelligence quotient, compared with mothers who consumed more than 340g per week (P=0.004). Low maternal seafood intake was also associated with increased risk of suboptimum outcomes for pro-social behavior, fine motor, communication and social development scores.

Innis et al, 2001 (positive quality) This was a prospective cohort study conducted in Canada to determine whether DHA levels in breastfed infants correlated with visual and neural development. Enrolled infants were exclusively breastfed for three months. Visual acuity was measured at two, four, six and 12 months, speech perception and object search task was measured at nine months, Bayley's mental development index and psychomotor development index was measured at six and 12 months, and novelty preference was measured at six and nine months. 83 infants were enrolled (39 male and 44 female); however, only 75 infants were exclusively breastfed for three months. Infant red blood cell (RBC) phosphatidylethanolamineDHA was significantly related to visual acuity at both two (R=0.32, P=0.01) and 12 (R=0.30, P=0.03) months of age. In addition, the ability to discriminate non-native retroflex and phonetic contrasts at nine months of age was related to the plasma phospholipid DHA (R=0.48, P<0.02) andRBC phosphatidyl-ethanolamine DHA (R=0.26, P=0.02) at two months of age.

Oken et al, 2005 (positive quality) This was a prospective cohort study conducted in the US to examine the associations of maternal fish and seafood intake and maternal hair mercury with six-month infant cognition in participants of Project Viva. Participants completed a semi-quantitative FFQ at 26 to 28 weeks of gestation, and maternal hair samples were collected during the hospitalization for the delivery. The FFQ was previously calibrated against blood levels of long-chain n-3 FAs and distinguished four categories of seafood consumption (canned tuna, shellfish/mollusk, dark/fatty fish, and lean/other fish). Infants underwent cognitive testing at approximately six months of age using the percent novelty preference on visual recognition memory testing. Of 211 mothers consenting to the hair sample,135 mother-infant pairs were included in the analysis. Mothers consumed an average of 1.2 fish servings per week during the second trimester and mean hair mercury was 0.55ppm, with 10% of samples having greater than 1.2ppm. Higher fish consumption in pregnancy was associated with better infant cognition, but higher mercury levels were associated with lower cognition; mean visual recognition memory score was 59.8 (range 10.9 to 92.5) and scores were highest among infants of women who consumed more than two weekly fish servings but had mercury levels less than 1.2ppm.

Oken et al, Am J Epidemiol 2008 (positive quality) This was a prospective cohort study conducted in the US to study associations between maternal fish intake, blood mercury levels and child cognition in participants of Project Viva. Participants completed a semi-quantitative FFQ at 26 to 28 weeks of gestation, and blood samples were analyzed during the second trimester visit. Children completed the Peabody Picture Vocabulary Test (PPVT) and the Wide Range Assessment of Visual Motor Abilities (WRAVMA) at three years of age. Three hundred forty-one mother-child pairs were included in the analysis. Mean maternal fish intake varied from 0 to 7.5 servings, with a mean intake of 1.5 servings per week. Higher fish intake was associated with better child cognitive test performance, and higher mercury levels with poorer test scores. Effect estimates for more than two weekly servings of fish intake vs. no intake were 2.2 §5% CI: -2.6 to 7.0) for the PPVT and 6.4 (95% CI interval: 2.0 to 10.8) for the WRAVMA, and for mercury in the top decile, the effect estimates were -4.5 (95% CI: -8.5 to -0.4) for the PPVT and -4.6 (95% CI: -8.3 to -0.9) for the WRAVMA. There was no benefit associated with fish consumption of less than two servings per week.

Oken et al, Am J Clin Nutr 2008 (positive quality) This was a prospective cohort study conducted in Denmark to examine

associations of maternal fish consumption during pregnancy and the duration of infant breastfeeding with attainment of child developmental milestones in participants from the Danish National Birth Cohort. Enrolled women completed semi-quantitative FFQ at gestation week 25, and were instructed to complete computer-assisted telephone interviews at gestation weeks 12 and 30, and at six and 18 months after delivery. Of 50,276 women completing the initial interview and FFQ, 35,557 women completed the six-month postpartum interview and 25,446 women completed the 18-month postpartum interview. Higher maternal fish intake and greater duration of breastfeeding were associated with higher child developmental scores at 18 months (OR=1.29, 95% CI: 1.20 to 1.38 for the highest vs. lowest quintile of fish intake and OR=1.28, 95% CI: 1.18 to 1.38 for breastfeeding more than 10 months compared to breastfeeding less than one month); these associations were similar for development at six months.

Olsen et al, 2006 (positive quality) This was a prospective cohort study conducted in Denmark to examine the association between seafood intake and risks of pre-term and post-term delivery. Women completed questionnaires regarding fish consumption during gestation weeks 16 and 30. 8,729 pregnant women were included in the analysis. When fish intake was based solely on intake reported during the first trimester, mean gestation length was shorter by 3.91 days (95% CI: 2.24 to 5.58) and odds of pre-term delivery were increased 2.38 times (95% CI: 1.23 to 4.61) in those who never consumed fish compared with those who consumed fish as a main meal and fish in sandwiches at least once per week. These measures were similar when fish intake was based on intake reported during the second trimester. In women reporting the same fish intake in both trimesters, those who never consumed fish had 8.57 days (95% CI: 5.46 to 11.7) shorter mean gestation and 19.6 times (95% CI: 2.32 to 165) increased odds of pre-term delivery compared to high fish consumers. However, odds of elective and post-term delivery were reduced by a factor of 0.33 and 0.34, respectively, in women who never consumed fish.

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Author, Year, Study Design, Class, Rating	Study Description/Duration	Study Population, Demographics	Intervention	Significant Outcomes	Limitations
Brenna JT, Varamini B et al, 2007 Study Design: Meta-analysis. Class: M Rating:		65 international studies. N=2,474 women.	Determined concentration of DHA and AA in breast milk from mothers consuming free-living diets.	In primary analyses, DHA=0.32 ±0.22% (range, 0.06% to 1.4%) and AA=0.47±0.13% (range, 0.24% to 1.0%), indicating DHA in breast milk is lower and more variable than AA. Highest DHA found in coastal populations with high seafood consumption. The correlation between DHA and AA was low (R=0.25, P=0.02), indicating a ↑ degree of variability in DHA:AA in breast milk samples.	Studies varied in sample sizes and infant ages
Colombo et al 2004 Study Design: Randomized Controlled Trial Class: A	DHA during pregnancy. 18-month follow-up.	350 mothers and infants enrolled to evaluate DHA supplement during last trimester on pregnancy outcomes. Of 70 infants	To determine relationship between DHA and development of attention measured through visual habitation in first year and during second year. Mothers were fed high-DHA eggs (135mg per day) or low-DHA eggs (35mg DHA per	Infants of ↑-DHA mothers showed an accelerated ↓ in looking (more rapid encoding) over the first year, ↑ examining and less distractibility in second year. Analyses of attention and distractibility during toddlerhood showed toddlers of ↑-DHA mothers	Relatively small sample size. DHA supplement did not affect maternal DHA levels in previous trial.

		provided valid data at each of three time points for visual habituation; 58 returned for a 12-month session and 49 returned for a 18-month session. Location: United States.	six and eight months for visual habitation and 12 and 18 months for free-play and distractibility.	performance on distractibility assessments.	
Drouillet et al 2009 Study Design: Prospective Cohort Study Class: B Rating:		2,002 women recruited; 1,805 women included in analysis; 464 overweight. Mean age: 29.1±4.9 years. Food intake assessed at 24 weeks and delivery. Location: France.	Studied on relationship between seafood consumption and fetal growth and potential effect of maternal overweight on relationship. FFQs completed at recruitment, <24 weeks, on intake in year before pregnancy and after delivery on intake in last trimester.	No association between seafood intake and fetal growth. For overweight women, ↑ consumption of seafood before pregnancy was associated with ↑ fetal biparietal and abdominal circumferences and anthropometric measures; from lowest to highest tertiles of intake, mean birthweight was 167g higher (P=0.002).	Study was not based on representative sample.
Hibbeln et al 2007 Study Design: Prospective Cohort Study Class: B Rating:	Avon Longitudinal Study of Parents and Children (ALSPAC). Eight-year follow-up.	Of 14,541 pregnancies in the ALSPAC cohort, 13,988 children survived for at least 12 months. 8,946 infants were included at baseline, 8,801 children were included at 81 months and 5,449 children were included at eight years. Location: United Kingdom.	Tested association between maternal seafood intake during pregnancy and neurodevelopmental outcomes in childhood. Maternal seafood consumption measured by self-completed, non-quantitative FFQ at 32 weeks. Gross and fine motor, communication and social skills scales derived from Denver Development Screening Test and completed by mothers at six, 18, 30 and 42 months. Strengths and Difficulties Questionnaire at 81 months. Intelligence quotient with	After adjustment for confounders, maternal seafood intake during pregnancy of <340g per week was associated with ↑ risk of children being in lowest quartile for verbal intelligence, compared with mothers who consumed >340g per week (P=0.004). ↓ maternal seafood intake was associated with ↑ risk of suboptimal outcomes for pro-social behavior, fine motor skills, communication and social development scores.	Maternal report of child development and behavior are prone to reporting bias.

			abbreviated WISC-III at eight years.		
Innis et al 2001 Study Design: Prospective Cohort Study Class: B Rating:	12-month follow-up.	83 infants enrolled (39 male and 44 female). Only 75 infants were exclusively breastfed for three months. Location: Canada.	To determine whether DHA is related to visual and neural development in term breast-fed infants. Infants exclusively breastfed for three months. Visual acuity was measured at two, four, six and 12 months, speech perception and object search measured at nine months, Bayley's mental dev index and psychomotor index measured at six and 12 months, and novelty preference measured at six and nine months.	Infant RBC phosphatidylethanolamine DHA was significantly related to visual acuity at two (R=0.32, P=0.01) and 12 (R=0.30, P=0.03) months. Ability to discriminate phonetic contrasts at nine months was related to plasma phospholipid DHA. (R=0.48, P<0.02) and RBC phosphatidyl-ethanolamine DHA (R=0.26, P=0.02) at two months.	None.
Oken et al 2005 Study Design: Prospective Cohort Study Class: B Rating:	Six-month follow-up.	Participants of Project Viva. Of 211 mothers consenting to hair sample, 135 mother-infant pairs were included. Location: United States.	Examined associations of maternal seafood intake and maternal hair mercury with six-month infant cognition. Subjects completed semi-quantitative FFQ at 26-28 weeks and maternal hair samples taken at delivery. Infants underwent cognitive testing at six months using percent novelty preference on visual recognition memory testing.	Mothers consumed an average 1.2 fish servings a week in second trimester and mean hair mercury was 0.55ppm. ↑ fish consumption was associated with better infant cognition, but ↑ mercury levels were associated with ↓ cognition; mean visual memory score was 59.8 (range, 10.9 to 92.5) and scores were highest among infants of women who consumed >two fish servings per week, but had mercury levels <1.2ppm.	↑ proportion of women who were educated, white and from a ↑ socioeconomic class.
Oken et al 2008 Study Design: Prospective Cohort Study Class: B Rating:	Three-year follow-up.	N=341 mother-child pairs. Participants of Project Viva. Location: United States.	Maternal fish intake, blood mercury and child cognition Studied the association between maternal fish intake, blood mercury levels and child cognition. Participants completed a semi-quantitative FFQ at 26 to 28 weeks and blood samples analyzed during second trimester visit. Children completed	Mean maternal fish intake varied from 0 to 7.5 servings, with a mean intake of 1.5 servings a week. ↑ fish intake was associated with better child cognitive performance, and ↑ mercury with poorer test scores. Effect estimates for >two fish servings a week vs. no intake were 2.2 (95% CI: -2.6 to 7.0) for PPVT and 6.4 (95% CI: 2.0 to 10.8) for	Study population contained a high proportion of women who were educated, white and from a higher socioeconomic class.

Okan at al	Participants from	Of 50 276	Peabody Picture Vocabulary Test (PPVT) and WRAVMA at three years.	For mercury in top decile, the effect estimates were -4.5 (95% CI: -8.5 to -0.4) for PPVT and -4.6 (95%CI: -8.3 to -0.9) for WRAVMA. No benefit associated with <two a="" fish="" servings="" th="" week.<=""><th>Subjects were</th></two>	Subjects were
Oken et al 2008 Am J Clin Nutr Study Design: Prospective Cohort Study Class: B Rating:	Participants from Danish National Birth Cohort. 18-month follow-up.	Of 50,276 women completing the initial interview and FFQ, 35,557 women completed the six-month postpartum interview and 25,446 women completed 18-month postpartum interview.	Studied associations of maternal fish consumption during pregnancy and duration of breastfeeding with child development. Women completed semi-quantitative FFQ at 25 weeks and completed interviews at 12 and 30 weeks and at six and 18 months postpartum.	↑ maternal fish intake and greater duration of breastfeeding were associated with ↑ child developmental scores at 18 months: OR=1.29, 95% CI: 1.20 to 1.38 for highest vs. lowest quintile of fish intake, and OR=1.28, 95% CI: 1.18 to 1.38 for breastfeeding >10 months compared to breastfeeding <one associations="" at="" development="" for="" month.="" months.<="" similar="" six="" td="" these="" were=""><td>Subjects were not a representative sample; women included in data analysis differed from those not included with respect to breastfeeding duration, marital status and smoking during pregnancy.</td></one>	Subjects were not a representative sample; women included in data analysis differed from those not included with respect to breastfeeding duration, marital status and smoking during pregnancy.
Olsen et al 2006 Study Design: Prospective Cohort Study Class: B Rating:	Length of pregnancy.	8,729 pregnant women. Location: Denmark.	Studied association between seafood intake in first and second trimesters and risks of pre-term and post-term delivery. Women completed questionnaires on fish consumption from weeks 16 and 30. Test diets: ~35% E from fat.	In first trimester, mean gestation length was shorter by 3.91 days (95% CI: 2.24 to 5.58) and odds of pre-term delivery ↑ 2.38-fold (95% CI:1.23 to 4.61) in those who never consumed fish, compared to those who consumed one serving a week. Measures similar in second trimester. In women reporting the same fish intake in both trimesters, those who never consumed fish had 8.57 days (95% CI: 5.46 to 11.7) shorter mean gestation and 19.6-fold (95% CI: 2.32 to 165) ↑ odds of pre-term delivery compared to high fish consumers. Odds of elective and post-term delivery were ↓ by a factor of 0.33 and 0.34, respectively, in women who never consumed fish.	Sample of pregnant women were not described in detail.

Research Design and Implementation Rating Summary

For a summary of the Research Design and Implementation Rating results, click here.

Worksheets

- Brenna JT, Varamini B, Jensen RG, Diersen-Schade DA, Boettcher JA, Arterburn LM. Docosahexaenoic and arachidonic acid concentrations in human breast milk worldwide. *Am J of Clin Nutr.* 2007; 85 (6): 1,457–1,464.
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- Innis SM, Gilley J, Werker J. Are human milk long-chain polyunsaturated fatty acids related to visual and neural development in breast-fed term infants? *J Pediatr*. 2001 Oct;139(4):532-8.
- Oken E, Wright RO, Kleinman KP, Bellinger D, Amarasiriwardena CJ, Hu H, Rich-Edwards JW, Gillman MW. Maternal fish consumption, hair mercury, and infant cognition in a U.S. Cohort. *Environ Health Perspect*. 2005 Oct;113(10):1376-80.
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